REMARKS

The Invention

Generally, the invention features compositions of neural stem cells that form non-adherent clusters in culture.

Rejections Under 35 U.S.C. 103(a)

The sole remaining rejection in this case in the rejection of all pending claims (claims 32, 33, 41-47, 49-52, and 54-60) as being obvious over Sosnowski et al. (Brain Res. 703: 37-48, 1995) in view of Anderson et al. (U.S. Patent No. 5,824,489). Applicants respectfully traverse this rejection on the basis that (i) there was no motivation to combine the cited references, and (ii) even if there were motivation, the two references do not teach or suggest every element of the claimed invention. Each of these points is addressed in turn.

There was no motivation to combine the teachings of Sosnowski and Anderson

Even if every element of the claims was taught or suggested by Sosnowski and Anderson (which they are not; see below), there would still be no motivation to combine the teachings of these references. The Examiner asserts that the motivation arises from Anderson's disclosure that neural crest stem cells "allows for the possibility of using said stem cells to treat peripheral neurological disorders in mammal, particularly humans." While the motivation to treat people suffering from neurological disorders is certainly a

motivation for searching for stem cells, this nonetheless is not a motivation to specifically combine the teachings of Sosnowski and Anderson. Sosnowski is merely studying the growth and development of olfactory neurons as a possible means of generating cells for use in autotransplantation into traumatized olfactory epithelium. As recognized by the Examiner, Sosnowski did not identify any cultured olfactory cells as being nestin-positive. Anderson, in contrast, describes the isolation of neural crest stem cells having, as one of their hallmarks, nestin immunoreactivity. One skilled in the art would simply not be motivated to look for Anderson's nestin-positive cells in Sosnowski's tissue.

As one would not be motivated to combine the teachings of Sosnowski with those of Anderson, applicants submit that the rejection of the claims as being obvious over these two references should be withdrawn.

The combination of Sosnowski and Anderson fails to teach or suggest every claim element

The claims as amended include four independent claims: claims 49-52. In each case, the combination of Sosnowski and Anderson fails to teach or suggest every claim element. This is discussed in greater detail below.

Claims 49 and 51

Claim 49 is directed to an isolated composition of neural stem cells of a mammal produced by isolating neural stem cells from mammalian peripheral tissue based on their

tendency to aggregate and form non-adherent clusters in culture. Claim 51 is directed to an isolated composition that includes a purified population of mammalian neural stem cells that form non-adherent clusters in culture. In each claim, the neural stem cells express nestin, are self-renewing, and are capable of producing dopaminergic neurons.

In order for claims 49 and 51 to be unpatentable over the combination of Sosnowski and Anderson, the two references must together teach or suggest every limitation of the claim. These two references fail to do so for at least two reasons, each of which is discussed below.

First, neither reference teaches or suggests isolating neural stem cells on the basis of their tendency to aggregate and form non-adherent clusters in culture. While the Examiner asserts that the cells of Sosnowski "were isolated...in a fashion similar to the cells claimed in the instant application," this simply isn't true. Sosnowski's cells are produced by enzymatic dissociation of the olfactory epithelium, followed by transfer to an appropriate culture vessel. Indeed, Sosnowski never produces an isolated composition of neural stem cells by any method; Sosnowski acknowledges that "[t]he dissociated tissue included mostly olfactory epithelium; however, also included were cells from respiratory epithelium, underlying lamina propria, periosteum and vascular tissue." (page 38, right column; emphasis added). Anderson similarly fails to teach or suggest isolating neural stem cells from peripheral tissue containing sensory receptors on the basis of the cells' tendency to aggregate and form non-adherent clusters. Anderson's cells are

adherent cells that required treatment with trypsin in order to detach them from the culture surface (see, e.g., column 19, lines 6-8).

Claims 49 and 51 further require that the claimed stem cells be capable of differentiating into dopaminergic neurons. Neither Sosnowski nor Anderson teaches or suggests that their olfactory cells or neural crest cells, respectively, are capable of differentiating into dopaminergic neurons. Sosnowski, for example, reports only the generation of GABAergic bipolar neurons, and is silent on the ability of the described olfactory cells from differentiating as dopaminergic neurons. Anderson similarly fails to teach or suggest that Anderson's cells are capable of differentiating as dopaminergic neurons.

In sum, Sosnowski and Anderson each fail to teach or suggest at least two limitations of claims 49 and 51. For this reason, applicants respectfully request that the rejection of these claims as being obvious over Sosnowski in view of Anderson be withdrawn.

Claim 50

Claim 50 is directed to an isolated composition that includes a purified population of mammalian neural stem cells that (i) form non-adherent clusters in culture, (ii) are self renewing, express nestin and glutamic acid decarboxylase (GAD), (iii) and can differentiate into cell types of the central nervous system.

Again, the combination of Sosnowski and Anderson fails to teach or suggest every limitation. As is discussed above for claims 49 and 51, neither reference suggests that the prior art cells formed non-adherent clusters in culture; only adherent cells are described by these two references. The combination of Sosnowski and Anderson also fails to teach or suggest the presence of GAD-positive cells, let alone cells that express GAD and nestin. As neither Sosnowski nor Anderson even suggests these claim elements, it follows that no combination of these two references can result in the claimed composition of claim 50. Applicants request that this rejection be withdrawn.

Claim 52

The fourth independent claim, claim 52, is directed to an isolated composition that includes a purified population of mammalian neural stem cells that form non-adherent clusters in culture, are self renewing, proliferate in an EGF-independent manner, and can differentiate into cell types of the central nervous system. Like the preceding three independent claims, claim 52 thus requires the presence of cells that form non-adherent clusters in culture. As is discussed above, the two references relied upon by the Examiner fail to describe such non-adherent cells. Sosnowski and Anderson also fail to describe another feature of the cells of claim 52: the ability to proliferate in an EGF-independent manner. Sosnowski and Anderson each culture their respective cells in the presence of EGF. In the case of Sosnowski, the EGF is provided as a component of fetal bovine serum (page 38, right column); Anderson adds recombinant EGF (column 15,

lines 9-10). As neither Sosnowski nor Anderson teach or suggest at least two elements of the claim, the rejection of claim 52 as being obvious over Sosnowski in view of Anderson should be withdrawn.

Conclusion

Effective immediately, please address all communication in this application to:

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Enclosed is a petition to extend the period for replying to the Office Action for three months, to and including June 4, 2003, and a check in payment of the required extension fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 6/4/03

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Marked-up version of claim 54 showing changes made

54. (Twice Amended) The composition of claim [claims] 50 [or 51], which neural stem cells can proliferate in an EGF-independent manner.